Skye Bioscience

Unlocking the pharmaceutical potential of the endocannabinoid system

September 2023

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Skye is researching the endocannabinoid system and strategically establishing a product pipeline based on first-in-class and only-in-class therapies with potential to positively affect diseases with significant prevalence and unmet needs

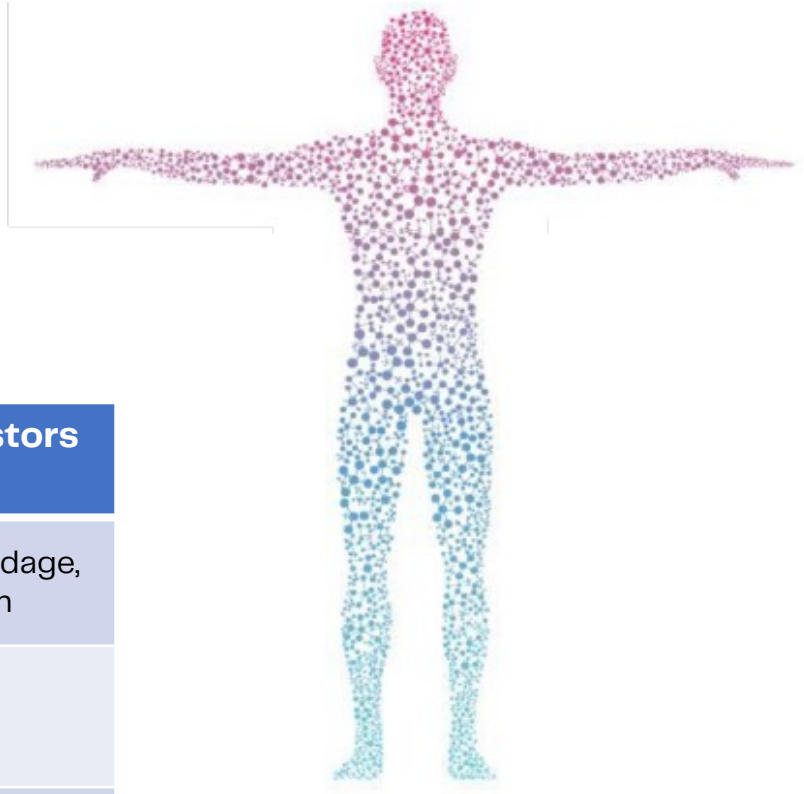
COMPELLING VALUE PROPOSITION

The right space, technology, team and investors

STRATEGIC FOCUS	Endocannabinoid system and particularly CB1 modulation have seen notable industry steps with well-positioned product development, strategic pharma acquisitions, and notable specialist healthcare investor support – including 5AM and Versant in Skye
NOVEL TECHNOLOGY	Portfolio of two distinct first-in-class, **only-in-class** CB1-targeting technologies: • Nimacimab: CB1 inhibitor to treat fibrotic, metabolic, and inflammatory-related diseases such as chronic kidney disease and NASH • SBI-100 OE: CB1 agonist/activator focused on reducing intraocular pressure (IOP) related to glaucoma/ocular hypertension
CLINICAL MILESTONES	Multi-compound endocannabinoid system-targeting development pipeline strategy with milestones from three separate studies over 18 months
EXPERIENCED TEAM	Expert board of directors, management and scientific advisors to pursue key catalysts and exit opportunities for products and company
INTELLECTUAL PROPERTY	Robust intellectual property and R&D pipeline to expand product pipeline and complement development strategy
COMMERCIAL POTENTIAL	Significant disease prevalence for each indication in development; multi-billion in aggregate addressing significant, distinct commercial opportunities

ENDOCANNABINOID SYSTEM: AN EMERGING FRONTIER

- Endocannabinoid system ("ECS") receptors throughout the body modulate and help maintain homeostasis of physiological functions. Over- or underactivation of these receptors is involved in an array of diseases
- ECS has many receptors that are viable therapeutic targets to beneficially modulate receptor signaling
- Interest in ECS as a target for drug development by small biotech, acquisition by pharmaceutical companies, and investment by specialist healthcare investors highlighted by past developments/transactions and recent ones below :

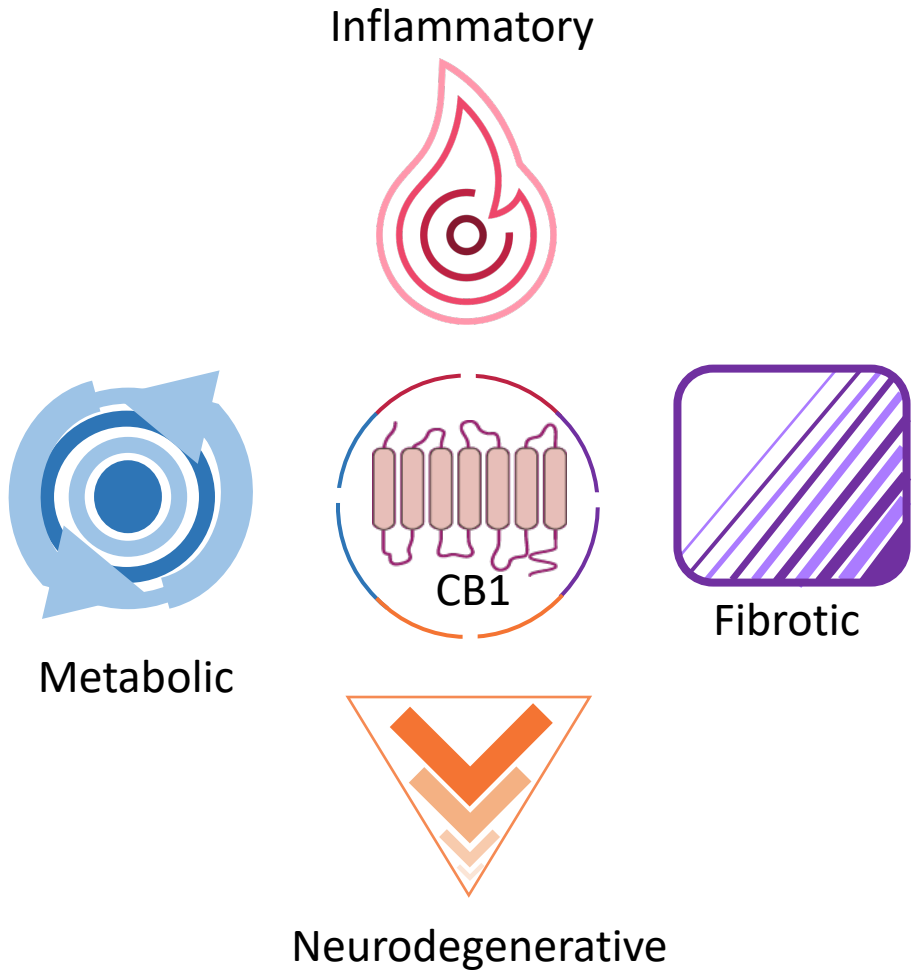


Company	Acquired by	Deal Value	Lead Asset	Healthcare Investors
GW pharmaceuticals	Jazz Pharmaceuticals Innovation that performs	$7.2B 2021	Epidiolex Natural CBD	Orbimed, Deerfield, Adage, Venrock, Farallon
Zynerba PHARMACEUTICALS	HARMONY BIOSCIENCES	Up to $140M 2023	Zygel Natural CBD	
inversago PHARMA	novo nordisk®	Up to $1.075B 2023	INV-202 CB1 inverse agonist	Deerfield, Farallon
Bird Rock Bio	skye BIOSCIENCE	$20M Aug, 2023	Nimacimab CB1 inhibitor	5AM Ventures, Versant Ventures

CB1: HIGH-POTENTIAL TARGET FOR PHYSIOLOGICAL REGULATION

CB1 involved in many disease processes

- Skye is researching multiple ECS targets but is initially focused on cannabinoid receptor 1 ("CB1")
- CB1 is a viable target as its modulation via agonism (activation) or inhibition can alter inflammatory, metabolic, fibrotic and neurodegenerative pathways to positively impact critical pathophysiological processes
- CB1 is most prevalent within the CNS but, in pathological states, the CB1 axis plays an important role in either promoting or blunting disease progression in peripheral tissues
- These tissues and associated pathology include the eye/glaucoma and kidney/chronic kidney disease, Skye's initial development focus



ADVANCING DISTINCT CB1-TARGETING THERAPEUTICS

Skye has two clinical-stage programs with multiple clinical inflection points

NIMACIMAB

MOA	Disease	R&D	Phase 1	Phase 2
CB1 Receptor Inhibitor *Sub-cutaneous*	Chronic Kidney Disease			

SBI-100 OE

MOA	Disease	R&D	Phase 1	Phase 2
CB1 Receptor Agonist *Topical*	Glaucoma			

Best-in-class and Only-in-class Molecules

Nimacimab – only CB1 negative allosteric modulator antibody in the clinic
SBI-100 OE – first/only prodrug of THC developed and currently in the clinic for glaucoma

Validated Targets/ Clear Clinical Endpoints

Nimacimab – proteinuria is an accepted surrogate for demonstrating improved kidney function for proof-of-concept
SBI-100 – lowering intraocular pressure (IOP) prevents subsequent progression of functional damage in the retina and is accepted as an approvable clinical endpoint

Favorable Safety Profiles

Both drugs designed to minimize safety issues associated with previous CB1 modulators, while maximizing clinical benefit of targeting this axis for disease modification.

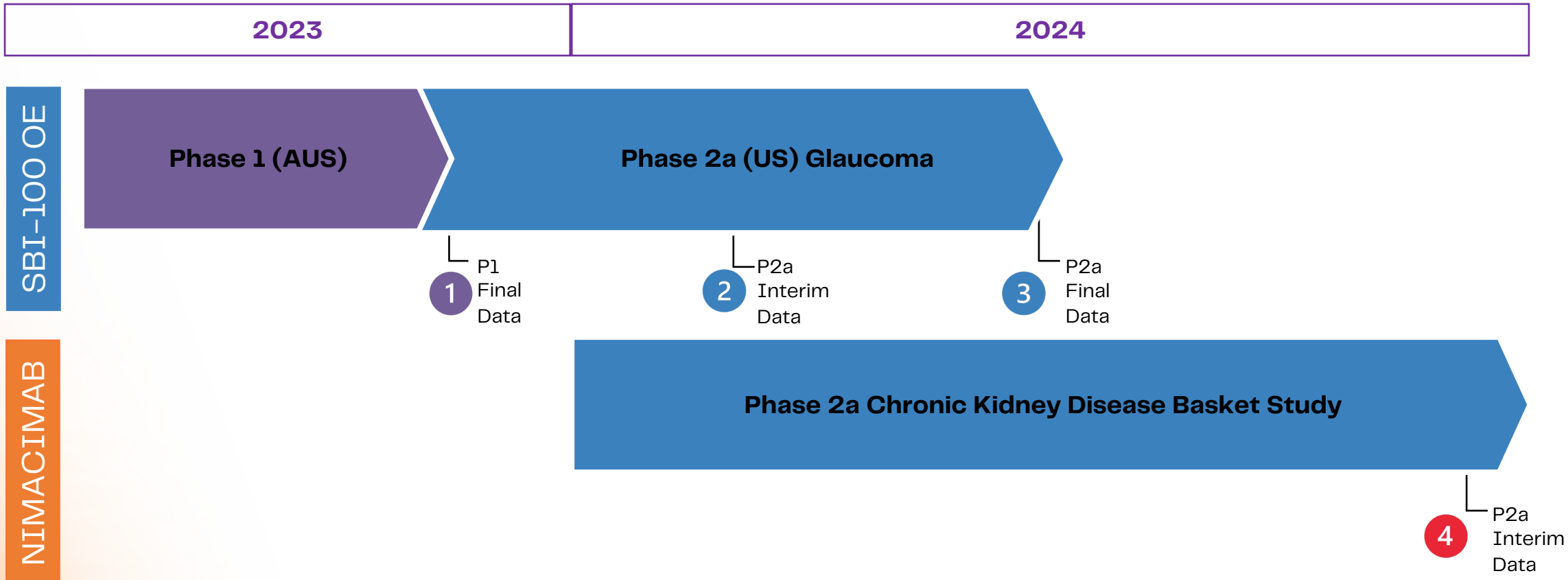
EXPLOITING PROVEN TARGETS WITH IMPROVED DRUG DESIGN

CB1 is a validated target for glaucoma and other inflammatory/fibrotic/metabolic diseases

Dynamics	Nimacimab	SBI-100 OE
Basic Goal	Reduce inflammatory, fibrotic and/or metabolic processes that cause other degenerative conditions in organs.	Reduce intraocular pressure in the eye. Potentially provide neuroprotection of optical nerve cells
History	Rimonabant validated CB1 receptor as effective target for obesity	Cannabis/THC known to reduce intraocular pressure since 1970s. Also known to protect against neurodegeneration.
Historic Challenge	Safety – depression due to CNS exposure	Safety – psychotropic effects due to CNS exposure, coupled with poor bioavailability in ocular tissue
Skye Improvements	New mechanism for CB1 inhibition: negative allosteric modulator Highly selective for CB1 receptor in the periphery (i.e. outside the brain); is not detected in CNS PK profile allows for favorable dosing regimen	Local delivery with eye drop in a novel formulation Prodrug design for improved bioavailability in the eye Designed for minimal/no psychotropic effect

ANTICIPATED CLINICAL MILESTONES

Working toward four data catalysts in two key programs through end of 2024



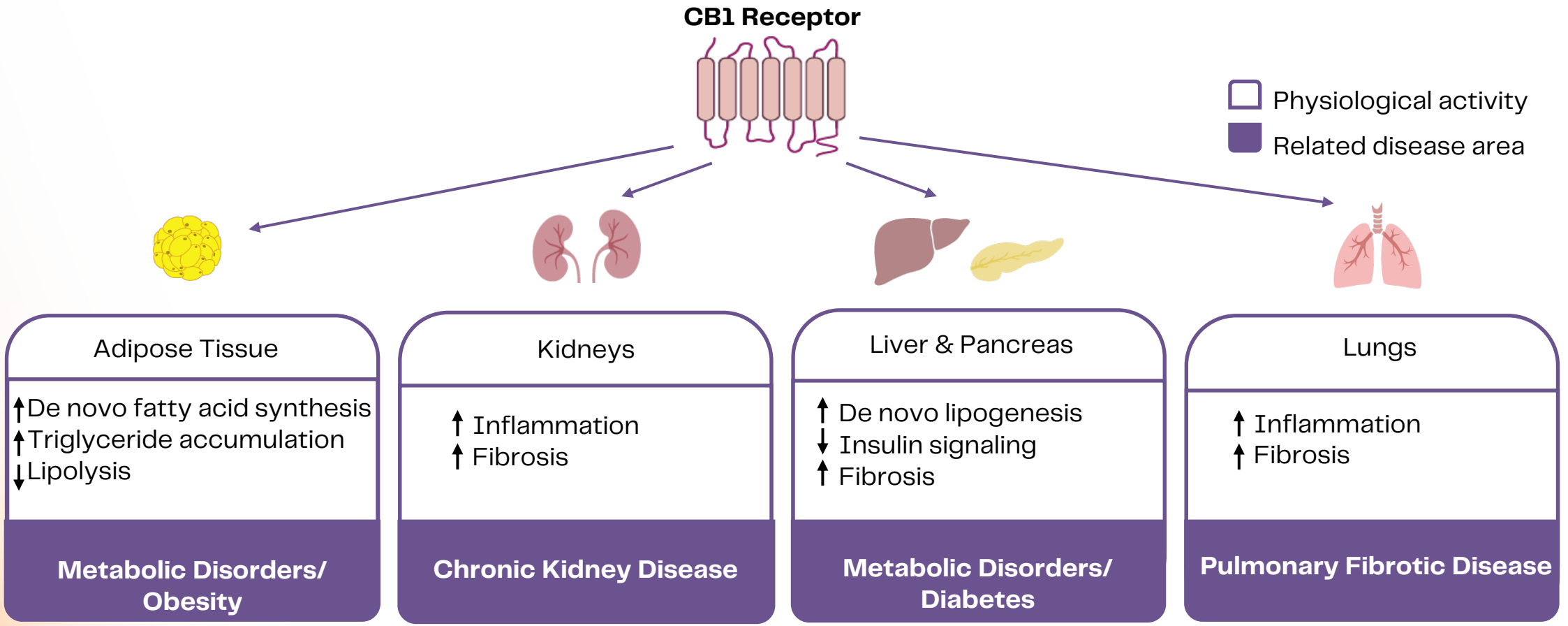
Nimacimab

Broad Potential.

Initial Focus on Chronic Kidney Disease

CB1 OVERACTIVATION: ROLE IN CRITICAL DISEASES

Upregulation of CB1 signaling involved in multiple inflammatory, fibrotic and metabolic diseases in various organs; significant prevalence and unmet needs



NEED FOR EFFECTIVE AND SAFE INHIBITION OF CB1 SIGNALING

- Early-generation CB1 inhibitors showed efficacy in models of obesity, pulmonary fibrotic diseases, fibrotic liver disease, and kidney disease
- But their therapeutic window was very limited, and central nervous system safety concerns were observed, including serious adverse effects such as anxiety and depression.
- Second-generation small molecule therapeutics have been developed to be more "peripherally restricted" to limit CNS exposure to the drug, but some may still have issues with CNS-related safety
- **We believe nimacimab, a new and distinct class of CB1 inhibitor, has the potential to become the leader in this space.**

NIMACIMAB: FIRST- & ONLY-IN-CLASS CB1 INHIBITOR

Unique mechanism of action to inhibit CB1 signaling; Phase 2-ready

- Humanized monoclonal antibody
  - Negative allosteric modulator
  - Inhibits ligand-mediated and intrinsic CB1 signaling
  - Highly selective for CB1, with no detectable binding of CB2 or other GPCRs
  - Mechanism of action in fibrotic, inflammatory and metabolic diseases
- Completed 3-week and 26-week toxicology studies with up to 75 mg/kg administered bi-weekly subcutaneously in cynomolgus monkeys; no accumulation of nimacimab in the brain and cerebral spinal fluid, even at doses significantly higher than the anticipated effective doses in humans
- Completed Phase 1 SAD study in healthy volunteers and MAD in non-alcoholic fatty liver disease (NAFLD) and diabetic kidney disease (DKD) patients; no impact on cognitive function or signs of anxiety or depression
- Open INDs for chronic kidney disease, NASH, gastroparesis
- Sufficient drug product available to support Phase 2a study

Data support the promise of safely and effectively targeting peripheral CB1 receptors to treat disease with nimacimab

CHRONIC KIDNEY DISEASE: ATTRACTIVE PATH FOR NIMACIMAB

Appealing development considerations

- All potential disease targets involving CB1 overactivation have significant unmet needs and large clinical and commercial opportunities
- Many have significant cost drivers or anticipated challenges with enrollment or speed to data
- Skye selected chronic kidney ("CKD") disease due to :
  - Ease of enrollment through basket study to evaluate multiple disease indications within CKD
  - Clear clinical endpoints, with relative low cost and speed, that would later be acceptable to potential partners and regulators
  - Existing open Investigational New Drug file with FDA
- Planning for Phase 2a basket study of multiple chronic kidney disease indications that would set the stage for Phase 2b study
- Evaluate multi-model mechanism of action of nimacimab
  - Enrollment criteria will include patients with BMI ≥ 30
  - Will allow for evaluation of weight-loss potential

CKD disease progress

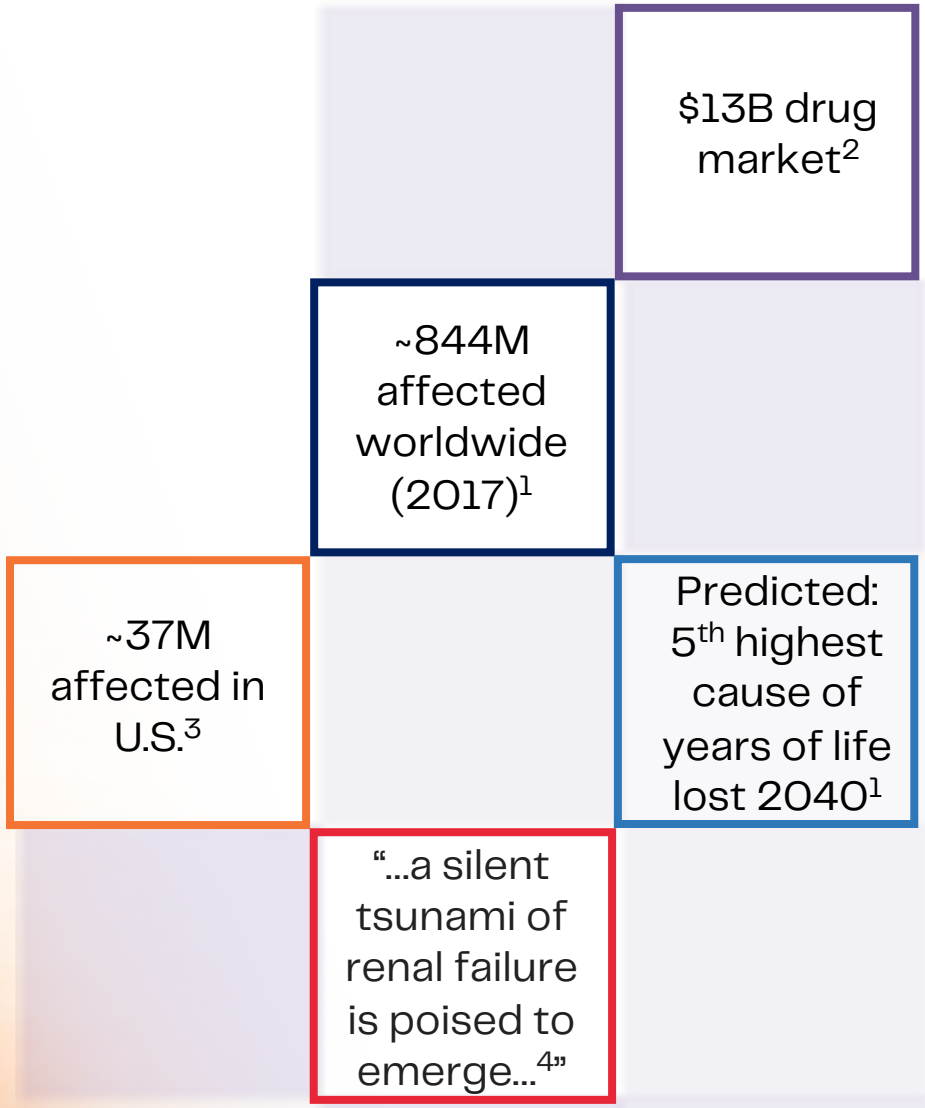
- Chronic kidney disease involves a combination of inflammatory, fibrotic, and metabolic processes.
- Fibrosis, is a hallmark of CKD progression. In response to ongoing damage and inflammation, the kidneys attempt to repair themselves by producing more connective tissue. The resulting formation of scar tissue can impair kidney function over time.
- Kidney function is commonly gauged using the estimated glomerular filtration rate (eGFR), a measure of the kidneys' ability to filter toxins or waste from the blood
- Additionally, proteinuria or albuminuria evaluation through urine analysis reflects the degree of renal damage and provides insights into the disease's progression.
- CB1 is highly expressed in kidney structures and represents a promising target to potentially slow the decline of kidney health in patients with CKD.

COMPELLING EVIDENCE: CB1 INHIBITION/NIMACIMAB & CKD

Preclinical and clinical data demonstrate CB1 affects metabolic, inflammatory and fibrotic pathways important in the development of chronic kidney disease and indicate nimacimab as a potential treatment

Parameters	CB1
Expression in human disease	Increased in CKD patient samples Increased in podocytes exposed to high glucose or angiotensin
Genetic linkage	Polymorphism associated with increased risk of CKD in humans
Clinical data	Inhibition improves hyperglycemia
Cellular data supporting effect on mesangial expansion, thickening of glomerular basement membrane, and glomerular sclerosis	Inhibition in podocytes maintains perm-selectivity and decreases inflammatory and fibrotic factors; in proximal tubular cells prevents hypertrophy; and in mesangial cells reduces inflammatory and fibrotic factors
Transgenic mice	Develop glomerular inflammation and fibrosis
Animal models of chronic kidney disease	Increased expression; inhibition improves microalbuminuria, metabolic parameters, inflammation and fibrosis in multiple animal models with multiple antagonists

TARGETING CKD: HUGE PREVALENCE & UNMET NEEDS



"Chronic kidney disease has emerged as one of the most prominent causes of death and suffering in the 21st century[1]."

1 *Epidemiology of chrionic kidney disease: an update 2022*, Kidney Int, 96 (2019), pp. 1048–1050, K.J. Jager, C. Kovesdy, R. Langham, *et al.*

2 Chronic Kidney Disease Drugs Market Analysis, Coherent Market Insights, October 2022

3Chronic Kidney Disease in the United States, 2021. Centers for Disease Control and Prevention, US Department of Health and Human Services; 2021.

4D*eveloping Treatments for Chronic Kidney Disease in the 21st Century*, Matthew D. Breyer, MD, and Katalin Susztak, MD, PhD, Semin Nephrol. 2016 Nov; 36(6): 436–447.

COMPETITIVE LANDSCAPE VALIDATING CB1 MOA

Nimacimab sets itself apart from other CB1 peripherally-targeted agents

	GFB-024	INV-202	NIMACIMAB
Molecule Type	Antibody	Small Molecule	Antibody
Allosteric Modulator	○	○	✓
Inverse Agonist	✓	✓	○
Favorable Safety Phase 1 data	✓	✓	✓
No CNS Accumulation Preclinical data	✓	○	✓
Minimal Immunogenicity	○	N/A	✓

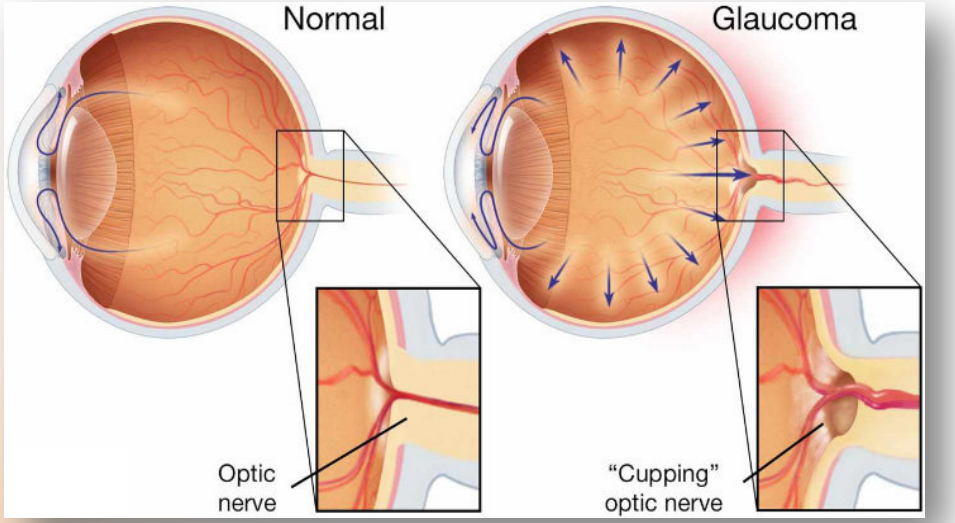
SBI-100 Ophthalmic Emulsion

Glaucoma Program

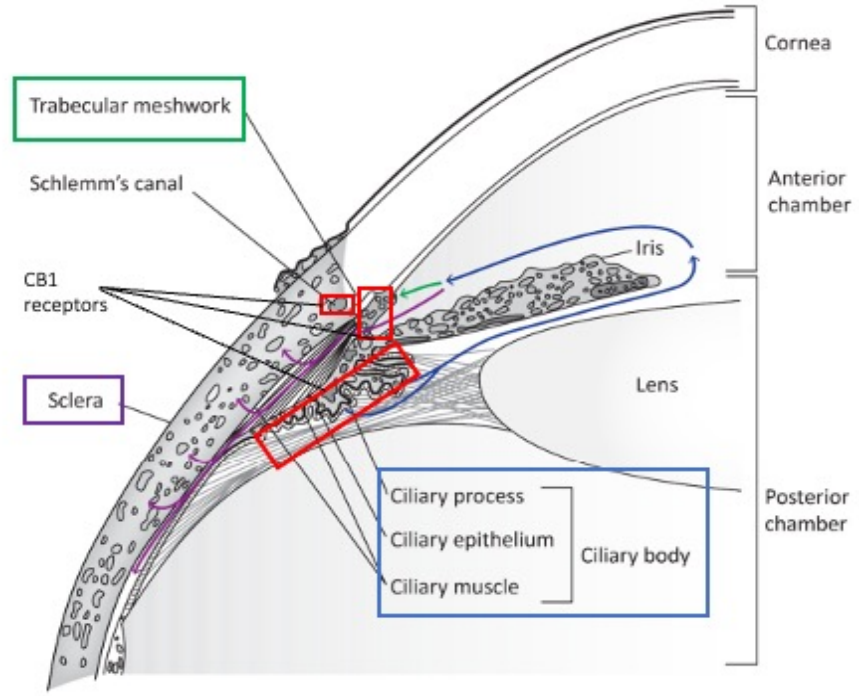
INCREASED INTRAOCULAR PRESSURE: KEY ROLE IN GLAUCOMA

Imbalanced aqueous humor inflow/outflow is key issue

- Aqueous humor **(blue)** provides nourishment and maintains shape of the eye. In healthy eye, production and drainage are balanced to maintain optimal intraocular pressure (IOP)
- Aqueous humor drained out of eye through trabecular meshwork **(green)** and uveoscleral pathway **(purple).** Inflammation and fibrosis in trabecular meshwork can diminish outflow of aqueous humor, increasing IOP.



Adapted from: Cairns et al, The Endocannabinoid System as a Therapeutic Target in Glaucoma. Neural Plasticity, 2016; Article ID 9364091



Existing glaucoma drugs focused on reducing IOP, but often have issues with reduced efficacy over time and patient tolerability

TARGETING GLAUCOMA: LARGE MARKET, UNMET NEEDS

One of the leading causes of irreversible blindness

$7B drug market

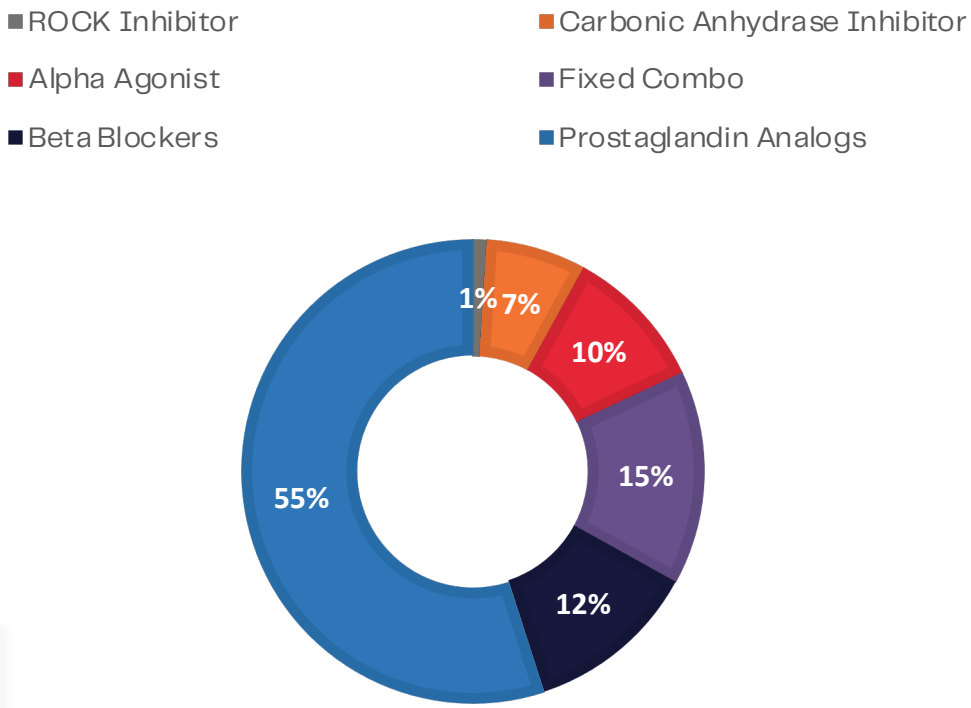
~60M patients worldwide

~110M patients by 2026

40% fail 1st line therapy[1]

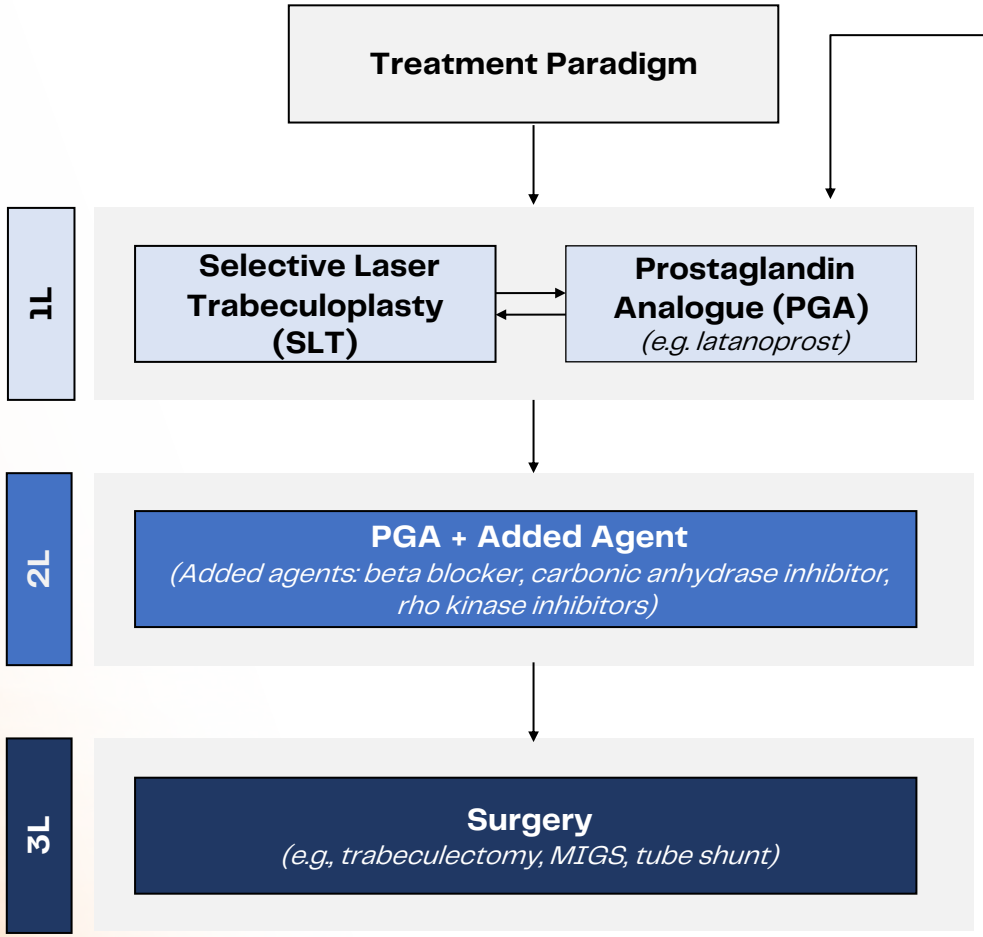
50% require 2 therapies[1,2]

Market predominantly uses legacy classes of drugs and generic compounds – lack of innovation!



1 Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. Arch Ophthalmolgy, 2010; 128:276–287
2 Lichter et al. Interim clinical outcomes in The Collaborative Initial Glaucoma Treatment Study Comparing initial treatment randomized to medications or surgery. Ophthalmology. 2001;108:1943–1953

CURRENT TREATMENT PARADIGM



Once ocular hypertension progresses to the point of requiring treatment, PGA IOP-lowering monotherapy becomes the dominant 1L treatment option

- **First-line treatment can either be a PGA monotherapy regimen or SLT;** use of SLT as an initial treatment option varies by practitioner, but it is suggested that SLT is more effective in mild patients[1,2]
- **PGA monotherapy is considered effective at reducing intraocular pressure ("IOP");** treatment is associated with eye irritation and redness
- If PGA monotherapy does not sufficiently reduce IOP, then a **PGA + alternative treatment combination therapy** (e.g., beta blocker, rho kinase inhibitor) is prescribed[2]

CLINICAL UNMET NEEDS IN GLAUCOMA

Physician input regarding key concerns and desires regarding glaucoma drugs

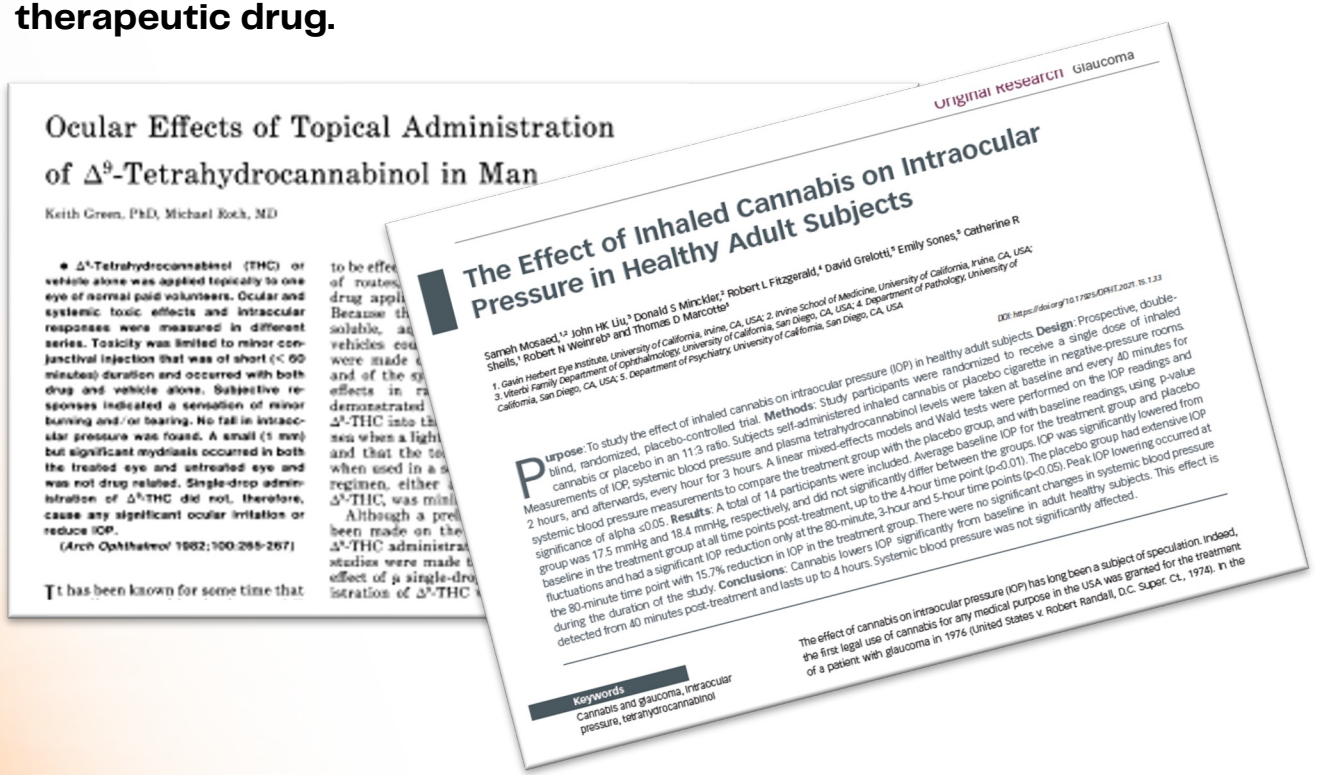
Key Unmet Needs	
1	**Patient Adherence:** Patient adherence is a **significant hurdle** KOLs face when providing effective long-term care; greater adherence with current pharmacologic options would allow KOLs to properly assess treatment efficacy
2	**More Efficacious 2L+ Agents:** Physicians often exhaust all pharmacologic treatments before recommending invasive surgical intervention; new **intraocular pressure-reducing 2L+ agents preferred to prevent or prolong the need for risky surgery**
3	**Unique Mechanism of Action:** An agent with a **different target** from current classes of drugs would allow for **more effective treatment** of "tough-to-treat" patients that often cycle through traditional therapies
4	**Neuroprotective Agents:** An agent that offers **optic nerve protection agnostic of IOP dependence** could alleviate moderate to severe patients from aggressive pharmacologic and surgical treatment regimens

Source: LifeSci Q1 2022 Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. Payers, N=3 Strategics)

POTENTIAL OF CB1 AGONISM AS NEW CLASS OF GLAUCOMA DRUG

CB1 agonists proven to reduce IOP; Skye's SBI-100 OE first to offer new approach

Ability of CB1 agonist to lower intraocular pressure well-established by animal studies and human clinical trials. Challenge to be overcome was deliverability, bioavailability, and reduction of side effects not viable in a therapeutic drug.



Ocular Effects of Topical Administration of Δ^9-Tetrahydrocannabinol in Man

Keith Green, PhD; Michael Roth, MD

• Δ^9-Tetrahydrocannabinol (THC) or vehicle alone was applied topically to one eye of normal paid volunteers. Ocular and systemic toxic effects and intraocular responses were measured in different series. Toxicity was limited to minor conjunctival injection that was of short (< 60 minutes) duration and occurred with both drug and vehicle alone. Subjective responses indicated a sensation of minor burning and/or tearing. No fall in intraocular pressure was found. A small (1 mm) but significant mydriasis occurred in both the treated eye and untreated eye and was not drug related. Single-drop administration of Δ^9-THC did not, therefore, cause any significant ocular irritation or reduce IOP.

(Arch Ophthalmol 1982;100:265-267)

It has been known for some time that

Original Research Glaucoma

The Effect of Inhaled Cannabis on Intraocular Pressure in Healthy Adult Subjects

Sameh Mosaed,[1,2] John HK Liu,[3] Donald S Minckler,[2] Robert L Fitzgerald,[4] David Grelotti,[5] Emily Sones,[5] Catherine R Sheils,[1] Robert N Weinreb[2] and Thomas D Marcotte[5]

1. Gavin Herbert Eye Institute, University of California, Irvine, CA, USA; 2. Irvine School of Medicine, University of California, Irvine, CA, USA; 3. Viterbi Family Department of Ophthalmology, University of California, San Diego, CA, USA; 4. Department of Pathology, University of California, San Diego, CA, USA; 5. Department of Psychiatry, University of California, San Diego, CA, USA

DOI: https://doi.org/10.17925/OPHT.2021.15.1.33

Purpose: To study the effect of inhaled cannabis on intraocular pressure (IOP) in healthy adult subjects. **Design:** Prospective, double-blind, randomized, placebo-controlled trial. **Methods:** Study participants were randomized to receive a single dose of inhaled cannabis or placebo in an 11:3 ratio. Subjects self-administered inhaled cannabis or placebo cigarette in negative-pressure rooms. Measurements of IOP, systemic blood pressure and plasma tetrahydrocannabinol levels were taken at baseline and every 40 minutes for 2 hours, and afterwards, every hour for 3 hours. A linear mixed-effects models and Wald tests were performed on the IOP readings and systemic blood pressure measurements to compare the treatment group with the placebo group, and with baseline readings, using p-value significance of alpha ≤0.05. **Results:** A total of 14 participants were included. Average baseline IOP for the treatment group and placebo group was 17.5 mmHg and 18.4 mmHg, respectively, and did not significantly differ between the groups. IOP was significantly lowered from baseline in the treatment group at all time points post-treatment, up to the 4-hour time point ($p<0.01$). The placebo group had extensive IOP fluctuations and had a significant IOP reduction only at the 80-minute, 3-hour and 5-hour time points ($p<0.05$). Peak IOP lowering occurred at the 80-minute time point with 15.7% reduction in IOP in the treatment group. There were no significant changes in systemic blood pressure during the duration of the study. **Conclusions:** Cannabis lowers IOP significantly from baseline in adult healthy subjects. This effect is detected from 40 minutes post-treatment and lasts up to 4 hours. Systemic blood pressure was not significantly affected.

Keywords: Cannabis and glaucoma, intraocular pressure, tetrahydrocannabinol

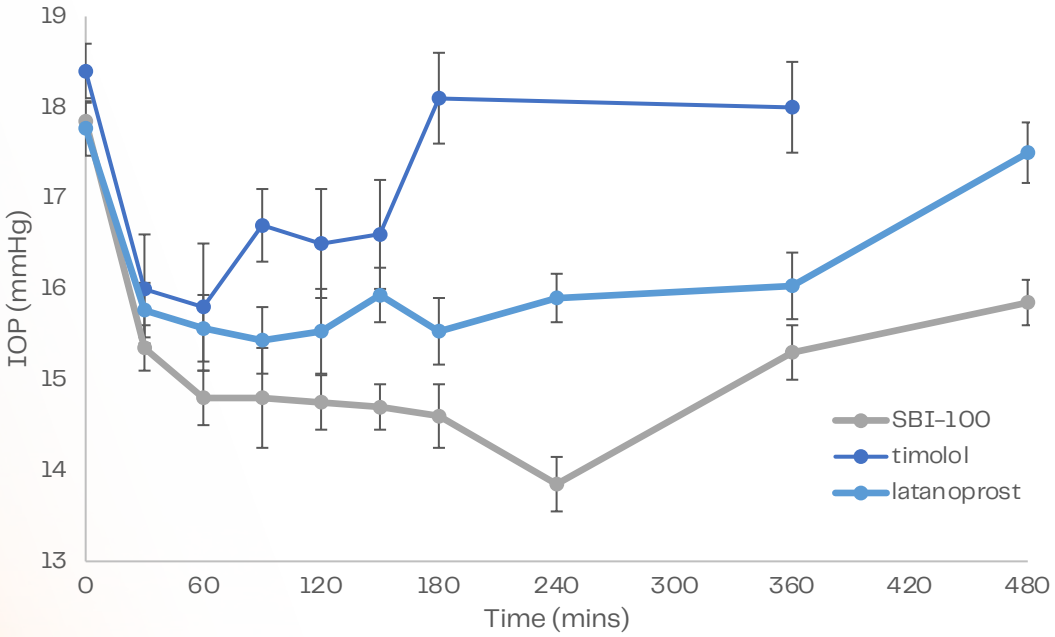
The effect of cannabis on intraocular pressure (IOP) has long been a subject of speculation. Indeed, the first legal use of cannabis for any medical purpose in the USA was granted for the treatment of a patient with glaucoma in 1976 (United States v. Robert Randall, D.C. Super. Ct., 1974). In the

SBI-100 Ophthalmic Emulsion ("OE"):

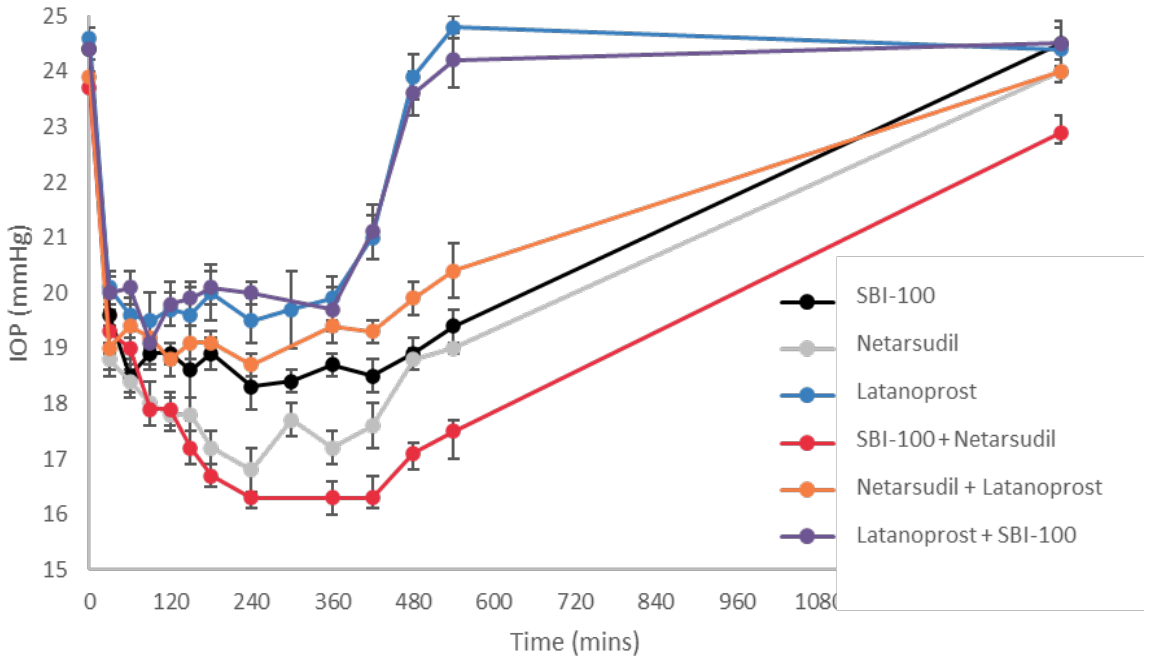
- **CB1 agonist (activator)**
  - **Highly selective for CB1**, with no detectable binding of CB2 or other GPCRs
  - Reduction of aqueous humor production
  - Improved aqueous humor outflow
  - Mechanism of action includes inflammation and neuroprotection
  - Combines well with approved therapies

SBI-100 OE DEMONSTRATES SUPERIOR IOP LOWERING

Nonclinical comparison with standard of care drugs shows favorable characteristics



In multiple preclinical studies, SBI-100 demonstrated superior IOP lowering compared to leading therapies as a **single agent**

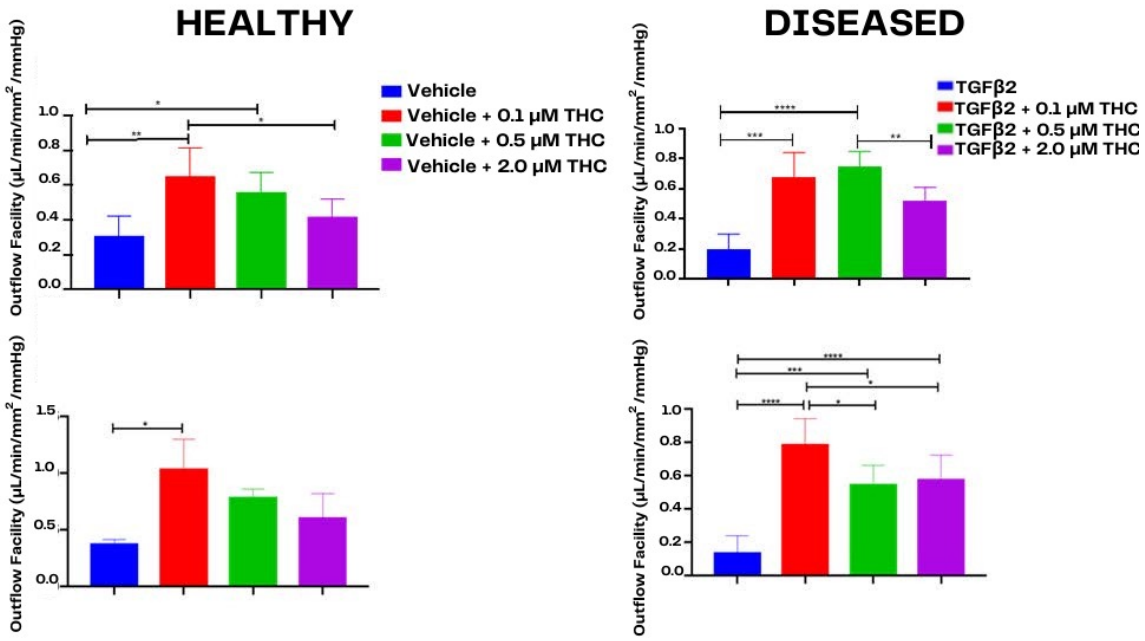


In preclinical studies, SBI-100 demonstrated enhanced efficacy when **combined** with other approved therapies

SUPPORTED BY OTHER INDICATORS OF UTILITY

Increased outflow via trabecular meshwork

- Restricted outflow through trabecular meshwork and fibrosis in tissue may be key to underlying pathophysiology of glaucoma
- In 3D model of human TM cells, **SBI-100's active pharmaceutical ingredient significantly increased outflow in both healthy and disease-simulated tissue**



Reduced markers of inflammation & fibrosis

- **SBI-100 significantly reduce markers associated with fibrosis and inflammation, drivers of glaucoma**
- Potentially disease-modifying through extracellular matrix remodeling of the trabecular meshwork
- Highlights multi-factorial mechanism of action, including anti-inflammatory and anti-fibrotic responses
- Potential new class of treatment with therapeutic attributes distinct from existing IOP-lowering drugs

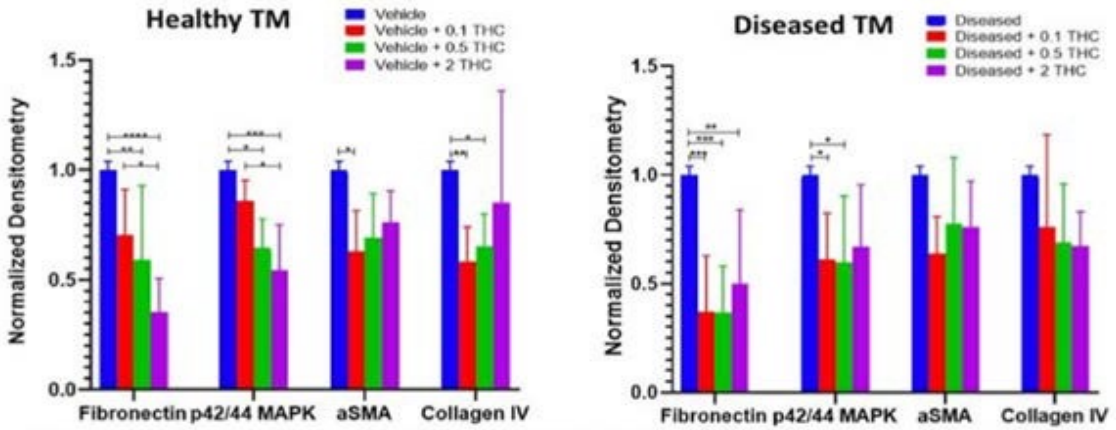


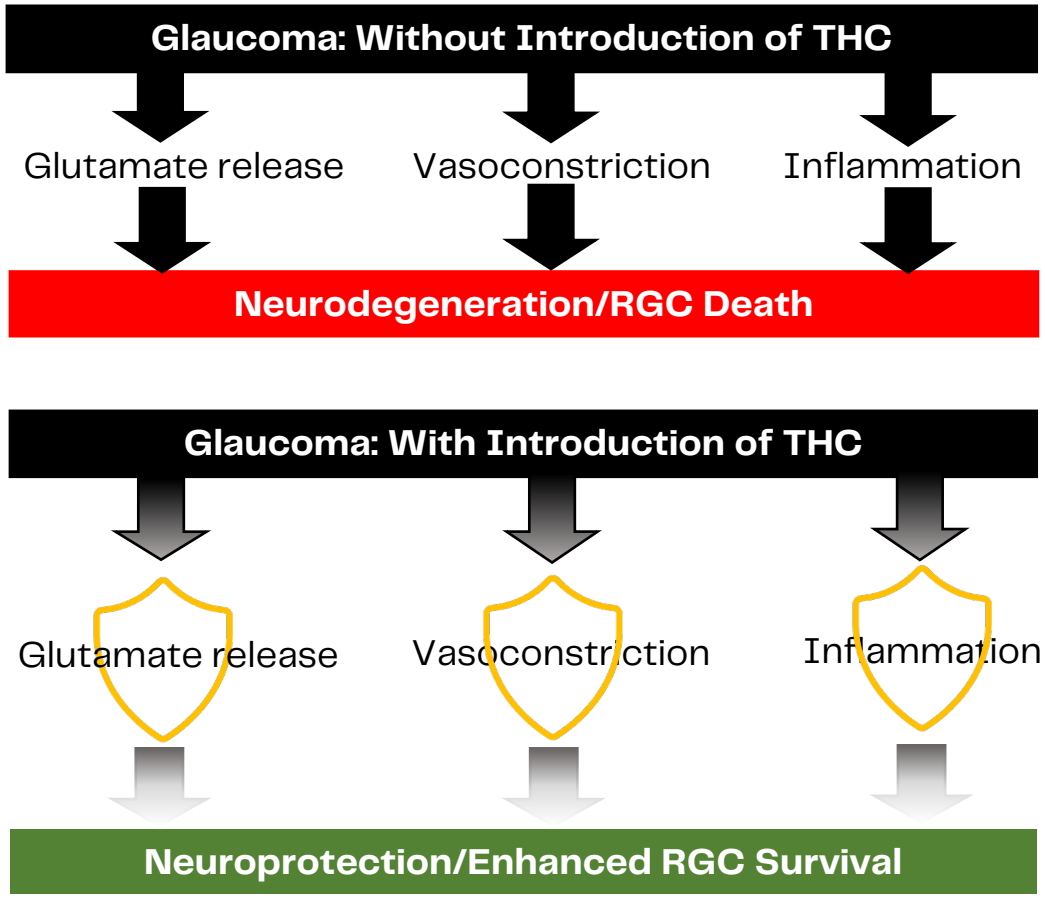
Figure 2. Protein analysis of markers linked to fibrosis at the 3D HTM after 6 days of treatment with THC. All samples of three donors were analyzed using Two-way ANOVA ****P<0.0001, ***P<0.001, **P<0.01, *P<0.05, N ≥ 4 per donor.

POTENTIAL NEUROPROTECTIVE BENEFITS

Research has identified key processes that lead to neurodegeneration and death of retinal ganglion cells (RGC):

- Destructive glutamate release[1]
- vasoconstriction of optic nerve[2]
- Inflammation[3]

SBI-100 OE active ingredient, THC, has shown ability to reduce neurodegenerative mechanisms and preserve RGCs[4]

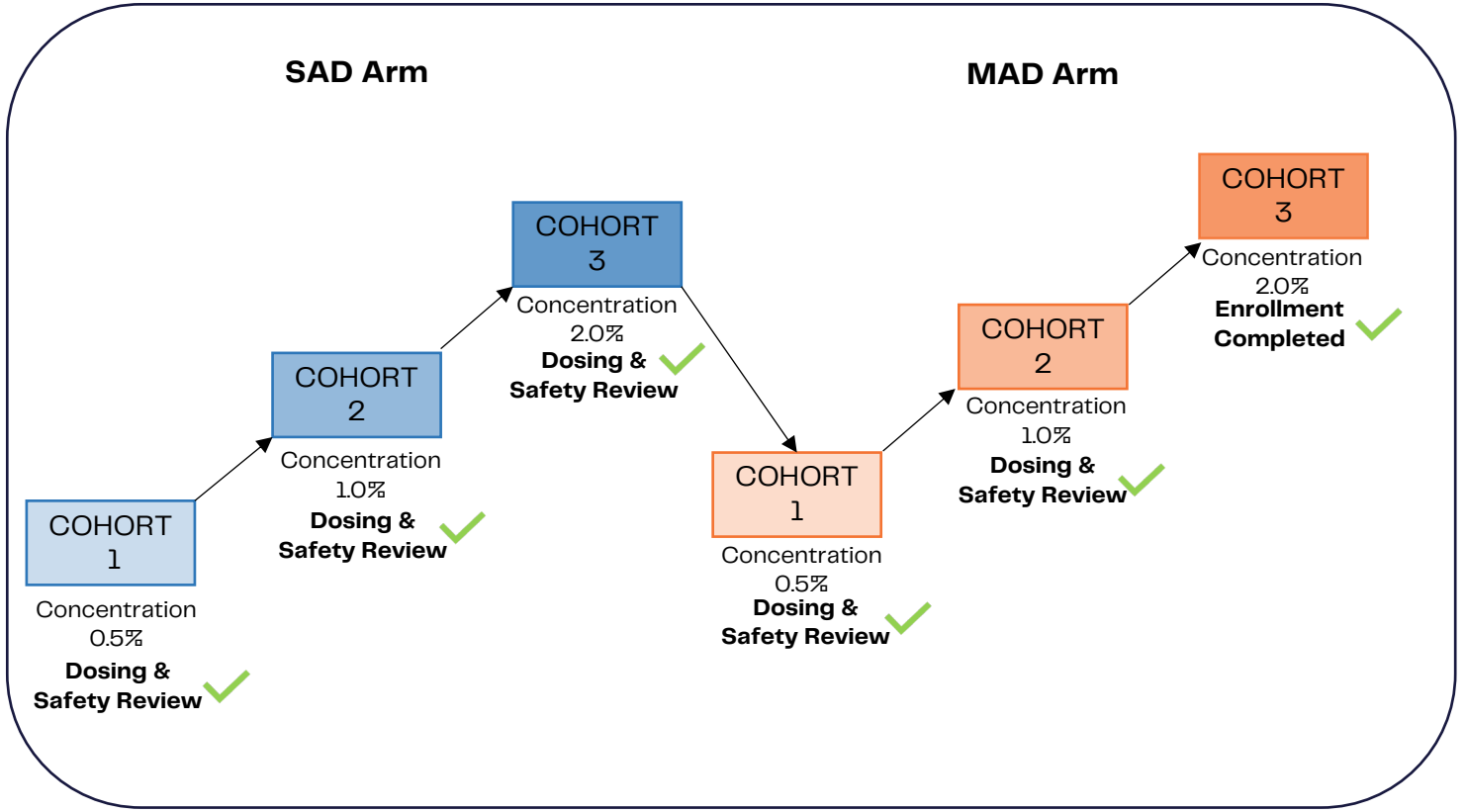


[1] El-Remessey et al, Am. J. Pathol. 2003 Nov;163(5):1997-2008
[2] Green et al, Exp.Eye Res. 1978;26:65-69
[3] Krishnan et al, Neuroscience. 2015;284:536-545
[4] Crandall et al, Ophthalmic Res 2007;39:69-75

PHASE 1 SAD/MAD ENROLLED; NO SERIOUS ADVERSE EVENTS

Dosing completed June 2023

- 14-day animal toxicology studies with up to 2% concentration administered daily topically in two different species
- Open IND for glaucoma with FDA
- Randomized, double-masked, placebo-controlled; evaluating safety and tolerability of topically administered SBI-100 OE or placebo on a single eye in ~48 healthy subjects
- Single ascending dose arm: 1 treatment, monitored 3 days. Multiple ascending dose arm: 2 treatments per day for 5 days, monitored 7 days
- As new chemical entity and regulated controlled substance, demonstrating safety is important to advance SBI-100 OE
- Preliminary safety review: **no adverse events of concern**
- Topline data Q3 2023



Study comprised 2 arms of 3 cohorts with 8 participants each (6 receiving SBI-100 OE and 2 placebo)

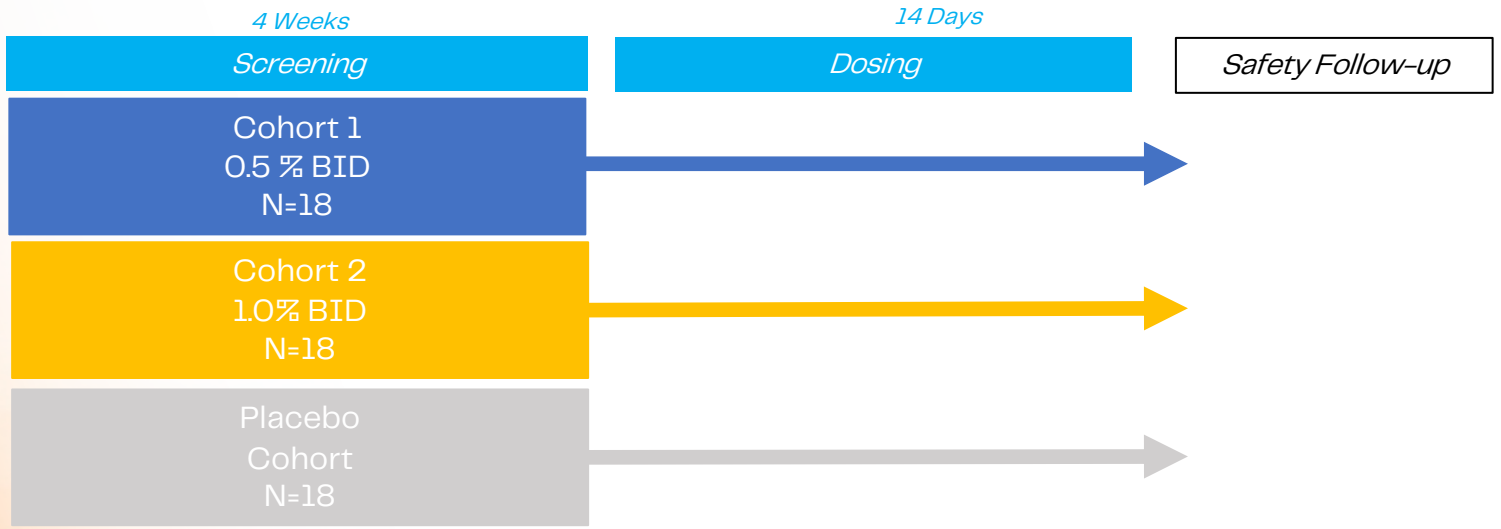
SBI-100 OE PHASE 2A GLAUCOMA PROOF-OF-CONCEPT STUDY

54 patients with primary open-angle glaucoma or ocular hypertension; start dosing Q4

Key Inclusion Criteria
- 21mmHg ≥ IOP < 34mmHg
- No prior surgical interventions for POAG or OHT

Primary Endpoint
- Change in diurnal IOP vs placebo

Secondary Endpoint
- Safety and tolerability
- Evaluation of psychotropic effects
- Change in diurnal IOP from baseline
- Exploratory biomarkers



Double-masked, placebo-controlled

- Plan for interim analysis and top-line results at 50% enrollment
- Exploratory biomarkers evaluating for ECS markers of response and markers of neuroprotection

SBI-100 OE: POTENTIAL TO FULFILL CLINICAL UNMET NEEDS

Following initial approval of topical drug format, Skye would explore innovative delivery technologies to improve patient adherence

SBI-100 satisfies two key unmet needs expressed by physicians

THC and other cannabinoids have demonstrated neuroprotective benefits in multiple models. This could be a future opportunity for SBI-100 OE

Key Unmet Needs in Glaucoma

✓	1	**Patient Adherence:** Patient adherence is a **significant hurdle** KOLs face when providing effective long-term care; greater adherence with current pharmacologic options would allow KOLs to properly assess treatment efficacy
✓	2	**More Efficacious 2L+ Agents:** Physicians often exhaust all pharmacologic treatments before recommending invasive surgical intervention; new **IOP-reducing 2L+ agents would be preferred to prevent or prolong the need for risky surgery**
✓	3	**Unique Mechanism of Action:** An agent with a **different target** from current classes of drugs would allow for **more effective treatment** of "tough-to-treat" patients that often cycle through traditional therapies
✓	4	**Neuroprotective Agents:** An agent that offers optic nerve protection **agnostic of IOP dependence** could alleviate moderate to severe patients from aggressive pharmacologic and surgical treatment regimens

Source: LifeSci Q1 2022 Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. Payers, N=3 Strategics)

PHYSICIAN FEEDBACK ABOUT SBI-100 OE

A new drug with novel mechanism of action would be well accepted by physicians

About SBI-100 OE's MOA

"I have conducted extensive research about [SBI-100's] mechanism and feel very confident it has a place in the treatment paradigm of OH and POAG. Many of my patients ask me about the IOP-reducing potential of THC."

"I am always willing to try a novel therapy given none of the existing options actually cure the disease. Given the unique mechanism of [SBI-100], I could see all of my patients receiving this option at some point throughout their disease course."

"[SBI-100] is a different mechanism and targeting a different receptor that could offer neuroprotective effect."

About SBI-100's Market Opportunity

*"Patients that are intolerant to PGA therapy are subjected to **less effective therapy options** with **greater side effect risk**. Ideally, I would want additional IOP-reducing agents that mechanistically have a different target to **avoid proven ineffective treatment approaches**."*

*"An aging US population represents a growing high-risk patient pool that will require treatment. If we don't **continue to innovate additional therapies** to treat a diverse group of patients, there will be a big problem in this country and globally."*

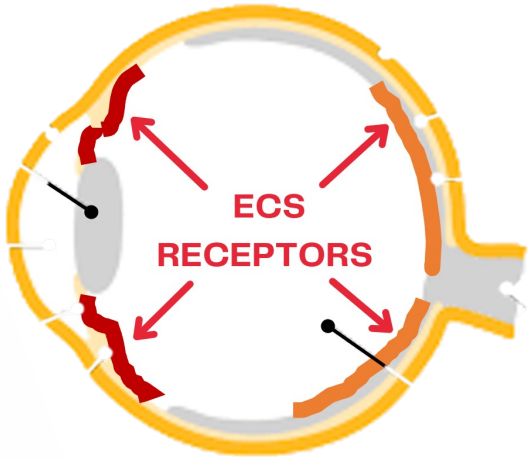
*"I use PGAs currently, but {SBI-100] **would probably be a second line** to latanoprost or used prior to timolol for patients that are little worried about side effects."*

*"A lot of patients are going to be **extremely happy** if I can provide them with multiple well-tolerated treatment options to reach target IOP reduction. Even if one agent is not enough, the different behaviors of the drugs give me the **added flexibility** I need to treat my patients."*

*"**More medications that are effective and safe will always be a need** until there is a cure for glaucoma. Especially for this product, being as effective as described would release patients from requiring 3 – 4 drops and **would make patient adherence easier**."*

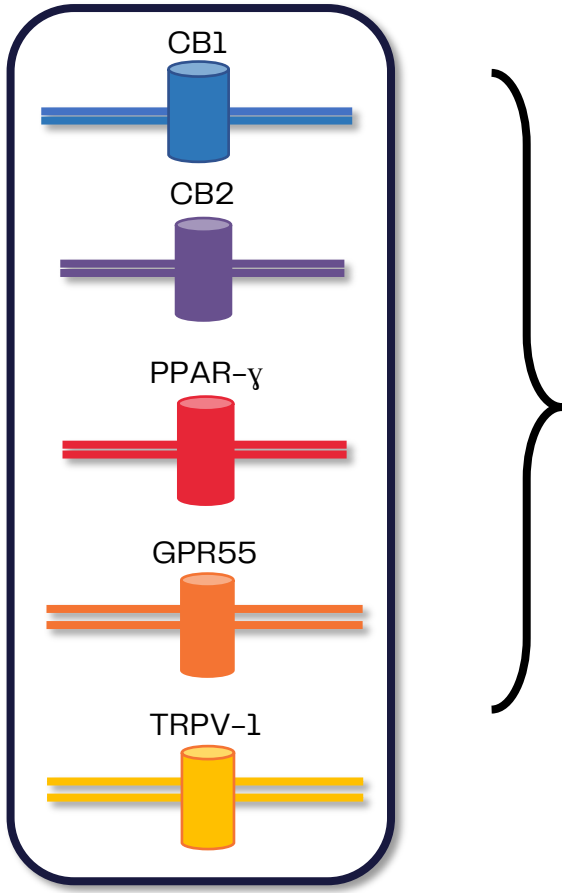
Source: LifeSci Q1 2022 Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. Payers, N=3 Strategics)

TARGETS TO EXPAND OPHTHALMOLOGY DRUG DEVELOPMENT



- ECS plays vital role in controlling array of functions in the body
- Affecting ECS may provide therapeutic benefit for multiple diseases, including in the eye
- ECS receptors found throughout eye shown to be involved in broad set of ocular functions and pathologies

ECS receptors in the eye



Relate to many ocular pathologies

- Intraocular pressure
- Nociception (pain)
- Inflammation
- Neovascularization
- Wound healing
- Neuroprotection
- Fibrosis
- Pain

Cannabinoid receptor–rich environment of eye creates an opportunity for drugs targeting these receptors to modulate ocular disease

Leadership, Financial Position & Next Steps

LEADERSHIP

Contributed to commercialization of 47+ drugs/diagnostics, led high-value strategic transactions and co-founded multiple companies

Executive Management

Punit Dhillon
CEO & Chair of BOD

Tu Diep, MSc
Chief Development Officer

Chris Twitty, PhD
Chief Scientific Officer

Kaitlyn Arsenault, CPA
Chief Financial Officer

Board of Directors

Andy Schwab
Managing Partner, 5AM Ventures

Deborah Charych, PhD
Co-founder and former CTO, RayzeBio

Keith Ward, PhD
Founder, Pres./CEO, & Chair, Kuria Therapeutics

Paul Grayson
Pres./CEO, Tentarix Bio; Versant partner

Praveen Tyle, PhD
Founder, Potens Pharma

Margaret Dalesandro, PhD
Pharma. Dev. Consultant, Brecon Pharma Consulting

CAPITALIZATION

Cap Table (proforma unaudited[1])

Common shares o/s	12.3 M
Options and RSUs	0.5 M
Warrants	3.3 M
Convertible note (as-converted basis)	1.0 M
Common shares f/d	17.1 M
Float[2]	3.2 M
Net New Capital Raised*	$8.4M

*Excludes $9 million in restricted cash posted as appellate bond

skye BIOSCIENCE

OTCQB SKYED*

* till approximately Oct 5, then it will revert to SKYE

[1] Financial information regarding equity items as of 6/30 as reported in Q2 10-Q, giving effect to the Merger/PIPE/Warrant transaction on 8/18 as reported in Form 8-K Filing on August 21, 2023, and special equity awards issued on 8/24

[2] Bulk of new investment locked up for 12 months to August 2024

SKYE NEXT STEPS

Achieve SBI-100 OE/glaucoma proof-of-concept milestone; advance nimacimab into clinic with longer-term view toward franchise expansion

- SBI-100 OE Phase 1 glaucoma clinical data early Q4 2023
- SBI-100 OE Phase 2a glaucoma clinical trial first dosing Q4 2023
- Nimacimab Phase 2a chronic kidney disease clinical trial initiation Q1 2024
- SBI-100 OE Phase 2a glaucoma interim IOP data Q1 2024
- Continued in vivo studies, biomarker development, next-generation efforts
- Planned SBI-100 OE Phase 2b glaucoma clinical trial initiation 2024
- Following P2a proof of concept for nimacimab, potential for clinical expansion to additional inflammatory, metabolic and fibrotic disorders
- Maintain focused operational and clinical development strategy
- Selectively evaluate business development opportunities to advance product pipeline
- Plan R&D Day in fall of 2023

THANK YOU

To learn more, please contact:

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